AF/1644

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Appellants:	Bo Arthur Einar Tjellstrom, et al.	**Examiner:**	Jessica H. Roark
Serial No.:	09/925,671	**Art Unit:**	1644
Filed:	August 9, 2001	**Docket:**	11133Z
For:	ORAL IMMUNOGLOBULIN TREATMENT FOR INFLAMMATORY BOWEL DISEASE	**Dated:**	July 14, 2004

Confirmation No.: 3329

Commissioner for Patents
Alexandria, VA 22313-1450

RESPONSE TO NOTIFICATION OF NON-COMPLIANCE WITH 37 C.F.R. §1.192(c)

Sir:

In response to the Notification of Non-Compliance with 37 C.F.R. §1.192(c) dated July 6, 2004, Appellants submit three copies of a new Appellants' Brief in the above-identified appeal.

In the new Brief, Appellants have added headings for "Real Party in Interest" and "Related Appeals and Interferences," in compliance with 37 C.F.R. §1.192(c)(1) and (c)(2). In addition, Appellants have also revised the section of "Summary of the Invention"

CERTIFICATE OF MAILING UNDER 37 C.F.R. §1.8(a)

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Dated: July 14, 2004

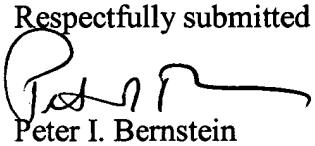
Peter I. Bernstein

to refer the specification by page and line number and to the drawing by reference characters in compliance with 37 C.F.R. §1.192(c)(5).

In view of the foregoing amendments, Appellants submit that the new Brief submitted herewith is in full compliance with 37 C.F.R. § 1.192(c). Early consideration of same is respectfully requested.

The Commissioner is hereby authorized to charge any fees which may be required, or credit any overpayment to Deposit Account No. 19-3886/RCT.

Respectfully submitted



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APPEAL BRIEF FOR APPELLANTS

Sir:

Appellants, through their attorneys, submit this Brief on Appeal pursuant to 37 C.F.R. §1.192 in response to the decision of the Examiner mailed on November 20,

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2003, finally rejecting Claims 1-10 and 13-14, and further in response to the Advisory Action mailed on February 23, 2004 ("the Advisory Action"), rejecting Claims 1-10, 13 and 15.

I. REAL PARTY IN INTEREST

Research Corporation of Technologies, Inc., a Delaware Corporation at 101 N. Wilmot Road, Suite 600 of Tucson, Arizona 85711-3365, is the real party of interest in the present appeal.

II. RELATED APPEALS AND INTERFERENCES

None.

III. STATUS OF THE CLAIMS

The present application as originally filed included Claims 1-14. Claims 11 and 12 have been withdrawn from consideration as directed to non-elected species. Responsive to the Final Action dated November 20, 2003 ("the Final Action"), Claim 14 was canceled and Claim 15 was added by an Amendment under 37 C.F.R. §1.116 dated February 6, 2004. Consequently, the claims on appeal are Claims 1-10, 13 and 15.

IV. STATUS OF THE AMENDMENTS

By Amendment under 37 C.F.R. §1.116 dated February 6, 2004, Appellants have argued that the rejection of Claims 1-10 under 35 U.S.C. § 102(e) is improper. It was further argued that the rejection of Claims 1-10 and 13-14 under 35 U.S.C. §103(a) was improper. By Advisory Action dated February 23, 2004, the Examiner entered the Amendment under 37 C.F.R. §1.116. The rejection of Claims 1-10

under 35 U.S.C. §102(e) was withdrawn and the rejection of Claims 1-10, 13 and 15 under 35 U.S.C. §103(a) was maintained.

Accordingly, the only rejection maintained for consideration on appeal is the rejection of Claims 1-10, 13 and 15 under 35 U.S.C. §103(a).

V. SUMMARY OF THE INVENTION

The present invention relates, *inter alia*, to the treatment of inflammatory bowel diseases (IBD) and mucosal inflammation, by oral administration of pooled human immunoglobulin preparation. See the specification, e.g., on page 5, lines 10-14 and on page 6, lines 9-21. IBD, such as ulcerative colitis and Crohn's disease, refers to serious, chronic disorders in the intestinal tract. See the specification, on page 1, lines 13-14.

The first embodiment of the present invention is exemplified in Claim 1 which recites a method for treating IBD by orally administering an effective amount of pooled human polyclonal immunoglobulin preparation to patients in need. The second embodiment of the present invention is exemplified in Claim 4 which is directed to treating mucosal inflammation by orally administering an effective amount of pooled human polyclonal immunoglobulin preparation to patients suffering from mucosal inflammation.

The present invention is based on the surprising discovery that the inflammatory process in IBD or mucosal inflammation can be affected from the luminal side of the gastrointestinal mucosa. Specifically, the present invention acknowledges that sufferers of IBD exhibit inflammation of the intestinal mucosa and submucosa, which

results in impaired mucosa barrier between enterocytes. See the specification on page 2, lines 23-29. Thus, the embodiments of the present invention are best exemplified by Examples 1-2 and depicted by Figures 1-2, in which patients treated with orally administered immunoglobulin exhibit an improved mucosa barrier. See the specification, on page 11, lines 13-26, Example 1 starting at page 12 and Example 2 starting at page 13.

Independent Claims 9-10 further delineate the content of immunoglobulin preparation of present invention and are supported by the specification, on page 6, line 22 to page 7, line 5, for example.

VI. ISSUES

The issue raised in the Final Rejection and the Advisory Action remaining for resolution on appeal is whether Claims 1-10, 13 and 15 are rendered obvious under 35 U.S.C. § 103(a) by the teachings of U.S. Patent No. 4,676,982 to Hassig ("Hassig") and U.S. Patent No. 4,477,432 to Hardie ("Hardie").

VII. GROUPING OF CLAIMS

Appellants respectfully submit that all of the rejected claims stand or fall together.

VIII. ARGUMENT

1. Introduction

The claims on appeal before the Board of Patent Appeals and Interferences ("the Board") are Claims 1-10, 13 and 15 and are set forth in the annexed Appendix. The claims are directed to treating inflammatory bowel diseases (IBD) or mucosal

inflammation by orally administering an effective amount of pooled human polyclonal immunoglobulin preparation to patients in need.

The subject matter of the present invention is patentably distinct from the separate and collective teachings of the prior art. The prior art references do not teach, disclose or even suggest the present invention. Moreover, there is no suggestion in the prior art to combine the references in the manner that the Examiner has recommended nor is there reasonable expectation of success that this specious combination would achieve the present invention. Notably, in fact, the present invention teaches away from the primary reference.

2. The subject matter of Claims 1-10, 13 and 15 is not rendered obvious by the combined teachings of Hassig and Hardie under 35 U.S.C. § 103.

In the Final Action dated November 20, 2003, the Examiner cited U.S. Patent No. 4,676,982 to Hassig ("Hassig") and U.S. Patent No. 4,477,432 to Hardie ("Hardie") in support of the rejection of Claims 1-10 and 13-14 under 35 U.S.C. § 103. In the Advisory Action, the Examiner maintained the rejection of Claims 1-10, 13 and the newly added Claim 15. Specifically, the Examiner has contended that one skilled in the art would have been motivated to substitute oral administration of immunoglobulin (IG), such as that described by Hardie, for intravenous administration of IG, as disclosed by Hassig, for treating IBD. The Examiner has also contended that by such substitution, one skilled in the art would have expected to achieve the present invention. The Examiner acknowledged that "Hardie teaches that oral administration of IG for the treatment of

intestinal infection was not only possible, but also advantageous." See, the Final Action, page 5, lines 1-2 of paragraph 4 (emphasis added).

As argued below, Appellants believe the Examiner's assertion to be erroneous since neither Hassig nor Hardie discloses, teaches or suggests the treatment of IBD or mucosal inflammation by oral administration of IG as claimed in the present invention.

The present invention, for the first time, recognizes that orally administered IG molecules are therapeutically effective for treating IBD.

The primary reference, Hassig, discloses a method of intravenously administering pooled, polyvalent IG to treat ulcerative colitis and Crohn's disease. There is no recognition in Hassig or any other reference cited on this record that IG can be orally administered, or that IG, even if orally administered, would still be therapeutically effective for treating IBD. There is certainly no recognition that IBD can be affected by IG on the luminal side of gastrointestinal mucosa, as disclosed in the present application.

Appellants maintain that in the absence of the requisite teaching of the present invention, one skilled in the art would not be motivated to treat IBD by orally administering intact IG which would otherwise be degraded and neutralized in the gut of the patient in need of treatment. Even assuming one skilled in the art would have been motivated to try, there would have been no reasonable expectation of achieving the present invention.

A rejection of claimed subject matter as obvious under 35 U.S.C. § 103 requires consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed device or composition, or carry out the claimed process; and (2) whether the prior art would have suggested that in so carrying out the claimed process, those of ordinary skill would have a reasonable expectation of success. *In re Vaeck*, 947 F.2d 488, 493, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991). There is no suggestion in the art of record to treat IBD by orally administering IG to patients in need, as disclosed by the present invention. Nor is there any expectation in the prior art on this record that orally administered IG can function for treating IBD.

Hassig explicitly states that IBD has an unknown etiology and is difficult to treat. While disclosing a method of treating IBD by intravenously administering IG, Hassig does not teach, or even suggest, that treatment of IBD can be achieved by orally administering IG to patients in need. In fact, Hassig was filed in 1986, two years after Hardie had been issued. Thus, Hassig would have been fully aware of Hardie's allegedly "advantageous" method which discloses that intact IG survives the gastrointestinal environment. Nevertheless, Hassig clearly acknowledges that IG is cleaved or degraded by pepsin. See Hassig, col. 1, lines 32-35. Appellants respectfully submit that it is undisputed and commonly known in the art that protein digesting enzymes, such as pepsin, are at high concentration in gastrointestinal tract of adults and children. Accordingly, Hassig not only fails to suggest that, as asserted by the Examiner, orally

administering IG is advantageous but also actually implies that IG would not remain intact in the gut because of the high concentration of pepsin therein. Clearly, there is no teaching, motivation or suggestion to combine Hassig with Hardie. When patentability turns on the question of obviousness, the search for and analysis of the prior art includes evidence relevant to the finding of whether there is a teaching, motivation, or suggestion to select and combine the references relied on as evidence of obviousness. *In re Lee*, 277 F.3d 1338, 1343, 61 U.S.P.Q.2d (BNA) 1430, 1433 (emphasis added).

Appellants observe that Hardie discloses that intact IG obtained from human blood, when administered orally, would not lose its therapeutic efficacy, i.e., would maintain a certain form of molecular integrity, such as secondary and tertiary structure. According to Hardie, the therapeutically effective IG is delivered (via oral administration) to the site where the therapeutic activity of the IG is required. Nowhere does Hardie teach or suggest that IBD requires the therapeutic activity of IG in the gastrointestinal tract. Indeed, nothing in Hardie even teaches or suggests treating IBD by IG, let alone treating IBD by orally administering IG to patients in need. Appellants note that the Examiner also admitted that Hardie does not teach that IG can treat IBD. In fact, Hardie discloses that orally administered IG "may be used in prevention or treatment of enteric infections . . . since intact IG with opsonic activity persisted in the gastrointestinal tract and thus is available to function in such prevention or treatment." See, Hardie, col. 7, lines 3-8.

It is well known in the art that the opsonic activity of antibodies, such as IG, involves guiding phagocytic cells to ingest and destroy the infection-causing bacteria by coating such bacteria with IG that would be recognized by the phagocytic cells. Appellant respectfully submit that enteric infection is known to be caused by bacteria or viruses in the intestine. IG, via opsonic activity, can guide phagocytic cells to destroy those bacteria or viruses. In other words, if retained intact in the gut, IG is required for treating enteric infection. However, one may not extrapolate the therapeutic activity of intact IG in treating enteric infection to treating other diseases affecting the gastrointestinal tract. Thus, Hardie does not ameliorate the deficiency of Hassig as to whether IG can function to treat IBD when orally administered.

Hassig clearly discloses that the etiology of IBD is unknown and is not simply caused by bacteria or viruses. Notably, the discovery of the present invention is not premised on the ground that IG remains complete intact in the gut. Thus, if degraded IG functions for treating IBD in the present invention, such a result is surprising in view of Hassig and Hardie. If orally administered IG remains intact in the gut, there is no suggestion that IG in the gut can function to affect IBD, based on the teachings of Hassig and Hardie. Indeed, as indicated above, the Examiner acknowledged that "the oral administration of immunoglobulin for the treatment of intestinal infection was . . . advantageous." One skilled in the art would not be motivated to combine a method for treating IBD by intravenously administering IG with a method which is advantageous merely for the treatment of infections by oral IG.

Moreover, Appellants observe that Hardie merely discloses that oral administration of intact IG prepared from human blood can treat intestinal infections in immature infants. Appellants note that Hardie assumes that to be effective, IG molecules must survive the gastrointestinal environment and reach their target areas with their biological properties intact. As argued in Appellants response to the Final Action, Appellants maintain that the gastrointestinal tract of an infant, which is much shorter and immature, is physiologically and biochemically different from that of an adult or a child, which carries a mature digestive system that readily degrade proteins, including IG. There is no teaching or disclosure in Hardie that orally administered IG can survive the gastrointestinal environment in adults and children. Indeed, it is both recognized by the references on this record and acknowledged by the Examiner that proteins will be digested in the gastrointestinal environment. In combining the teachings of Hassig and Hardie to achieve the present invention, one skilled the art must assume that IG would survive the gastrointestinal environment not only in immature infants, but also in adults and children. This type of extrapolation is both unwarranted and unfounded by the references on this record. Alternatively, one skilled in the art has to assume that degraded IG can still function for treating IBD, which is flatly contradicted by the disclosures of Hassig and Hardie, which explicitly require intact IG for efficacy.

In her rejection, the Examiner has improperly presumed that IG would remain intact in the gut of adults and children and such intact IG can function in the gut to treat IBD. Such presumptions are either formed with the distinct benefit of hindsight

based on the teaching of the present invention, or based on the Examiner's own belief or some other unknown authority. In fact, IBD has an unknown etiology. Thus, treatment of IBD may or may not require that IG molecules remain completely intact in the gut. In considering obviousness in patent applications, the factual question of motivation is material to patentability, and cannot be resolved on subjective belief and unknown authority. It is improper, in determining whether a person of ordinary skill would have been led to a combination of references, simply to use that which the inventor taught against its teacher. *In re Lee*, 277 F.3d at 1343, 61 U.S.P.Q.2d (BNA) at 1434.

It is only with the benefit of the present application that the Examiner establishes a nexus between the claimed invention and the cited prior art teaching. However, "[d]etermination of obviousness cannot be based on the hindsight combination of components selectively culled from the prior art to fit the parameters of the patented invention. There must be a teaching or suggestion within the prior art, or within the general knowledge of a person of ordinary skill in the field of the invention, to look to particular sources of information, to select particular elements, and to combine them in the way they were combined by the inventor." *ATD Corporation v. Lydall, Inc.*, 159 F.3d 534, 546, 48 U.S.P.Q.2d 1321, 1329 (Fed. Cir. 1998).

Even assuming, *arguendo*, that one skilled in the art was motivated to combine the teachings of Hassig and Hardie at the time the present application was filed, there would have been no reasonable expectation of success of achieving the present invention. One skilled in the art would not have reasonably expected that an IG

preparation, when administered orally, was possible to function effectively in the adult or juvenile gut for treating IBD. Both Hassig and Hardie acknowledge that, like other proteins, IG molecules can be degraded by the enzymes in the gastrointestinal tract. On the other hand, it would be completely unexpected that the successful treatment of IBD results from degraded IG in the gut.

Appellants acknowledge that Hardie states that the treatment of infections by orally administered IG was surprising because the IG molecule would be expected to be readily degraded in the stomach. See Hardie, at col. 2, lines 24-32. However, Appellants note that Hardie incorporates the teachings of numerous prior art references, which disclose that a composition comprising IG, if administered orally, only functions to protect against or treat infections in infants (e.g., Jelliffe, *Amer. J. Clin. Nutr.*, 29, 1227, 1976), newborn piglets (U.S. Patent No. 4,096,244), newborn calves (U.S. Patent No. 3,975,517) and other baby animals. Hardie relates to treatment of intestinal infections in "immature infants." Appellants respectfully direct the Board's attention to the fact that unlike newborns and infants, who do not have mature digestive systems that are required to digest proteins, adults and children have digestive systems that can digest proteins, including IG. Thus, by combining the prior art on this record to achieve the present invention, one has to assume that IG would remain intact in the guts of adults and children. Such an assumption is a sheer speculation. Notably, such an assumption is inconsistent with the disclosures of Hardie and Hassig. As indicated above, both Hassig and Hardie recognize that proteins, including IG, can be cleaved or degraded in the

(mature) digestive system. In fact, proteins, such as insulin and antibodies or IG, are usually administered parenterally (intravenously or intramuscularly) to avoid degradation in the digestive system. For example, insulin that can be orally administered is still not commercially available.

Further, even assuming IG would have remained intact in the gut of adults and children, one skilled in the art could only guess as to whether or not the intact IG in the gastrointestinal tract could function to treat IBD. The present invention does not require IG to remain intact in the gut for efficacy. The primary reference merely teaches that IG in the bloodstream can function to treat IBD. The secondary reference neither suggests the present invention nor ameliorates the deficiencies of the primary reference. Indeed, the present invention is based on the surprising discovery that IG can treat IBD from the luminal side of gastrointestinal mucosa. Even if IG would have survived the environment in gut, there is no recognition in the references of record that IG can affect IBD from the luminal side of gastrointestinal tract. Absent the teachings of the present invention, the result of treating IBD by orally administered IG would be, at best, unpredictable. Appellants also notes that both Hassig and Hardie state that degraded IG would not function. Thus, even if IG is degraded in the gut, it would be a surprise, in view of Hassig and Hardie, that IBD can be treated by orally administered IG.

The Examiner has offered no record that suggests that an IG preparation would be therapeutically effective in the gut for treating IBD. There is no reasonable expectation that treating a disease such as IBD, a disease having an unknown etiology,

would be achieved by directing IG to the gut where there is high concentration of protein digesting enzyme.

Appellants note that the Examiner has asserted that Hardie discloses that oral administration of IG is not only possible but also advantageous over intravenous administration. Appellants, however, respectfully maintain that the advantage of oral administration of IG, as taught by Hardie, is merely an advantage for the Hardie method. Appellants respectfully direct the Board's attention to the fact that the advantages of oral administration taught by Hardie, as admitted by the Examiner, are mere avoidance of injection or pain, which are very general and not specifically related to administering IG. Such advantages might be an important consideration in the context of Hardie's method, for treating infant patients. The same assertion may not be true, however, in other circumstances. For example, intravenous administration may be advantageous for chemotherapy drugs because of faster and better absorption, even though the patients have to suffer pain associated with the injection. Notably, the etiology of infection was well known long before Hardie, to be caused by bacteria or viruses. In contrast, the etiology of IBD was not known at the time the present invention was filed. Where, as here, the cause of IBD is unknown, an assertion that oral administration of IG would be advantageous for IBD treatment must be based on sheer speculation.

In combination with Hassig, the Examiner has cited Hardie as exemplifying that oral administration of IG can be substituted for intravenous administration of IG in the method of Hassig. However, Hardie merely teaches that

molecular integrity is "believed to be required for therapeutic effectiveness." Stated differently, Hardie teaches that molecular integrity may be necessary for IG's therapeutic effectiveness. Hardie does not teach or suggest intact IG is sufficient for treating IBD when administered orally.

Appellants strongly disagree with the Examiner's proposition that it would be expected that IG would treat other enteric diseases, such as IBD. For example, because the cause of colon cancer is not fully understood, one skilled in the art would not have a reasonable expectation, based on Hardie, that IG in the gut can function for treating colon cancer. Similarly, IBD's etiology is also unknown. Appellants submit that at best, Hassig and Hardie simply provide a possibility that since IG in the bloodstream can treat IBD, orally administered IG might also affect IBD. However, such possibility appears based on nothing more than wild guesses or wishful thinking, just as one could also wish that orally administered IG might treat colon cancer. In this regard, Appellants note that the Examiner seems to be of the opinion that, based on Hassig and Hardie, it is obvious for one skilled in the art to try treating IBD with orally administered IG. Appellants submit that this is a textbook "obvious to try" situation. However, "the court emphasizes that "obvious to try" is not the standard under 35 USC 103. As stated in *In re Eli Lilly and Co.*, . . .[a]n "obvious-to-try" situation exists when a general disclosure may pique the scientist's curiosity, such that further investigation might be done as a result of the disclosure, but the disclosure itself does not contain a sufficient teaching of how to obtain the desired result, or that the claimed result would be obtained if certain directions

were pursued." *Ex parte Goldgaber*, 41 USPQ 2d 1172, 1177 (B.P.A.I. 1996) (quoting *In re Eli Lilly and Co.*, 902 F.2d 943, 945, 14 USPQ 2d 1741, 1743 (Fed. Cir. 1990))

Thus, based on the teaching of the prior art on the record, one skilled in the art at the time the present application was filed would not have a reasonable expectation of success of employing IG, even for treating intestinal infections in adults, let alone for treating IBD in the patients including adults.

The leap from opsonic activity of IG for treating infection in infants to some unknown activity of IG in the gut for treating IBD is of quantum magnitude. Accordingly, any connection between treating enteric infection by orally administering IG to the infants' guts and treating IBD by intravenously administering IG to both adults and children is purely coincidence. Based on Hassig and Hardie, a conclusion that IG can be functional in the gut and function for treating IBD would rest on speculation or conjecture.

Appellants submit that the sheer speculation based on the teaching of Hassig and Hardie fails to meet the standard of obviousness under 35 U.S.C. § 103. *In re Fine*, 837 F.2d 1071, 1075, 5 U.S.P.Q.2d 1596, 1599 (Fed. Cir. 1988). At most, such speculation provides nothing more than an invitation to experiment; however, it is axiomatic that an invitation to try is not the standard under 35 U.S.C. § 103. *In re O'Farrell*, 253 F.2d 894, 903, 7 U.S.P.Q.2d 1673, 1681 (Fed. Cir. 1988).

In addition, the present invention teaches away from the primary reference. Appellants observe that the present application discloses that the method for treating IBD

by intravenously administering IG, had generated inconsistent results. See, the specification, on page 4, line 30 to page 5, line 3, which cites Levine D.S., et al., 1992 (*Am. J. Gastroenterol.* 87:91-100); Wolf A., et al., 1988 (*Mschr. Kinderheilk* 136:101-103); Knoflach P., et al., 1990 (*Ann. Intern. Med.* 112:385-386); Schmidt, C., 1990 (*Klinikarzt* 19:552-558); and Canva-Delcambre, V. 1996 (*Aliment. Pharmacol. Ther.* 10:721-727). Indeed, one of the objectives of the present invention is to overcome the problems and disadvantages of such methods as the one disclosed in Hassig.

Furthermore, there had been a long-felt need for an effective treatment method for IBD at the time the present invention was filed. The present invention provides a successful solution to this long-standing problem. The hypothetical combination of the cited references is not likely to defeat an invention where the evidence shows that long-standing problems were solved. *Kalman v. Kimberly-Cark Corp.*, 713 F.2d 760, 774, 218 U.S.P.Q. 781, 791 (Fed. Cir. 1995). The consistent criterion for determination of obviousness is whether the prior art would have suggested to one of ordinary skill in the art that this process should be carried out and would have a reasonable likelihood of success, viewed in the light of the prior art. Long-felt need in the face of prior art later asserted to lead to a solution tends to negate the proposition that the combination of such prior art would have been obvious. *Micro Chem., Inc. v. Great Plains Chem. Co.*, 103 F.3d 1538, 1547, 41 U.S.P.Q.2d, 1238, 1245 (Fed. Cir. 1997) (emphasis added). Thus, by solving a long-standing problem, the present invention is not obvious in view of Hassig and Hardie.

Accordingly, Claims 1-10, 13 and 15 are not rendered obvious by the teachings of the cited references.

3. The Examiner has improperly used hindsight arguments to reject the claims under 35 U.S.C. § 103.

Appellants respectfully submit that the Examiner has utilized the considerable benefit of hindsight in suggesting that it would have been obvious to employ oral administration of IG, as described by Hardie, in the method of using intravenous IG for the treatment of IBD, as described by Hassig, to successfully achieve the present invention. The Court of Appeals for the Federal Circuit in *In re Bond*, 910 F.2d 831, 834, 15 U.S.P.Q.2d 1566, 1568 (Fed. Cir. 1990) held that "obviousness cannot be established by combining the teachings of the prior art to produce the claimed invention absent some teaching, suggestion or incentive supporting the combination." See also, *Texas Instruments Inc. v. U.S. Int'l Trade Commission*, 988 F.2d 1165, 26 U.S.P.Q.2d 1018 (Fed. Cir. 1993).

Although the aforementioned arguments have been elucidated during the course of prosecution, the Examiner has maintained the Final Rejection, citing passages of Hassig and Hardie allegedly necessary to teach the features relied upon.

The claimed invention embodies a method for treating IBD comprising orally administering IG molecules to patients in need . The Examiner offered no reference that suggests orally administered IG in the gut could still function for treating IBD. Hassig, which is directed to treating IBD by administering IG intravenously, does not

suggest administering IG orally. Thus, the primary reference cited by the Examiner fails to teach or even remotely suggest the essential embodiment of the claimed invention.

Furthermore, while disclosing a method of orally administering intact IG, the secondary reference, Hardie, does not teach that IG remains functional in the gut of adults and children. Nor does Hardie disclose that IG in the gut can function for the treatment of IBD. Specifically, Hardie merely shows that IG molecules remain intact in the gut of immature infants. Hardie also explicitly admits that IG in the gut merely functions for treating enteric infections. Thus, the Examiner has offered no reference on this record which suggests orally administered IG would remain functional in the gut and funtion for treating IBD, as disclosed by the present invention.

It is well settled that in determining obviousness, the inquiry is not whether each element of the invention existed in the prior art, but whether the prior art made obvious the invention as a whole for which patentability is claimed. *Hartness International, Inc. v. Simplimatic Engineering Company*, 819 F.2d 1100, 2 U.S.P.Q.2d 1826 (Fed. Cir. 1987). One skilled in the art would not look to the teachings of Hassig and Hardie in order to achieve the present invention, whether in combination, or otherwise; and the Examiner has proved no convincing reason why such combination would be obvious to the skilled artisan. None of the cited references provide any incentive or encouragement to combine the references as recommended by the Examiner; nor does this specific combination result in the claimed invention. Accordingly, it is improper for the Examiner to combine the cited references, where the references do not suggest such a

combination, in order to reject Appellants invention under 35 U.S.C. § 103. *ACS Hospital Systems, Inc. v. Montefiore Hosp.*, 732 F.2d 1572, 1577, 221 U.S.P.Q. 929, 933 (Fed. Cir. 1984).

The Court of Customs and Patent Appeals in *In re Wesslau*, 353 F.2d 238, 147 U.S.P.Q. 391 (CCPA 1965), reversed a hindsight rejection and stated:

> The ever present question in cases within the ambit of 35 U.S.C. § 103 is whether the subject matter as a whole would have been obvious to one of the ordinary skill in the art following the teaching of the prior art at the time the invention was made. It is impermissible within the frame work of section 103 to pick and choose from any one reference only so much of it as will support a given position, to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one of ordinary skill in the art.

353 F.2d at 241, 147 U.S.P.Q. at 393 (emphasis added).

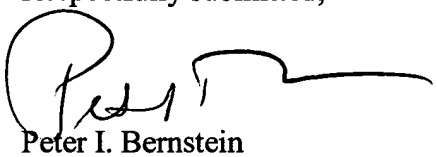
Again, as stated by the CCPA in *In re Imperato*, 486 F.2d 585, 587, 179 U.S.P.Q. 730, 732 (1973) ". . . the mere fact that those disclosures can be combined does not make the combination obvious unless the art also contains something to suggest the desirability of the combination." Appellants respectfully submit that the Examiner impermissibly chose bits and pieces from the prior art references and combined those bits and pieces in a manner not remotely suggested by the references themselves. There is absolutely no indication to combine Hassig with Hardie.

4. Conclusion

For all the foregoing reasons, it is believed that the Examiner's Final Rejection of Claims 1-10, 13 and 15 under 35 U.S.C. §103 constitutes reversible error. It

is, therefore, respectfully requested that the Board reverse the Examiner's rejection and pass the claims on appeal to allowance.

Respectfully submitted,



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IX. APPENDIX

CLAIMS ON APPEAL

1. (Previously presented) A method of treating inflammatory bowel disease (IBD) in a patient in need thereof which comprises orally administering to the patient an effective amount of a pooled human polyclonal immunoglobulin preparation.

2. (Original) The method according to Claim 1 wherein the inflammatory bowel disease is ulcerative colitis (UC).

3. (Original) The method according to Claim 1 wherein the inflammatory bowel disease is Crohn's disease.

4. (Previously presented) A method of treating mucosal inflammation which comprises orally administering to a patient suffering from said mucosal inflammation an effective amount of a pooled human polyclonal immunoglobulin preparation.

5. (Original) The method according to any one of Claims 1-4 wherein the immunoglobulin is at least one of immunoglobulin G (IgG), immunoglobulin A (IgA) or a mixture of immunoglobulin G (IgG) and immunoglobulin A (IgA).

6. (Original) The method according to any one of Claims 1-4 wherein the immunoglobulin preparation is dispersed in a pharmaceutically acceptable carrier.

7. (Original) The method according to any one of Claims 1-4 wherein the amount of immunoglobulin administered to said patient is from about 0.5 to 1.5 grams at least once a day.

8. (Original) The method according to any one of Claims 1-4 wherein the immunoglobulin is enterically coated.

9. (Previously presented) A method of treating inflammatory bowel disease (IBD) in a patient in need thereof which comprises orally administering to the patient a pooled human polyclonal immunoglobulin preparation comprising at least about 25% IgG antibodies.

10. (Previously presented) A method of treating mucosal inflammation which comprises orally administering to a patient suffering from said mucosal inflammation a pooled human polyclonal immunoglobulin preparation comprising at least about 25% IgG antibodies.

11. (Withdrawn) A method of treating inflammatory bowel disease (IBD) in a patient in need thereof which comprises orally administering to the patient a pooled human polyclonal immunoglobulin preparation comprising at least about 30% to about 85% IgG, about 5% to about 30% IgA and about 1% to about 25% IgM polyclonal antibodies.

12. (Withdrawn) A method of treating mucosal inflammation which comprises orally administering to a patient suffering from said mucosal inflammation a pooled human polyclonal immunoglobulin preparation comprising at least about 85% IgG, about 5% to about 30% IgA and about 1% to about 25% IgM polyclonal antibodies.

13. (Previously presented) The method of any one of Claims 1, 4 or 9-10 wherein said pooled human polyclonal immunoglobulin preparation comprises immunoglobulins pooled from human individuals.

14. (Cancelled)

15. (Previously presented) The method of any one of Claims 1, 4 or 9-10 wherein said pooled human polyclonal immunoglobulin preparation is non-antigen specific.